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ON THE SPECIFIC DYNAMIC ACTION OF PROTEIN

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In a previous communication[1] evidence was presented that the normal excretion of nitrogen by the mammalian kidney is attended by a relatively great expenditure of energy, which in man amounts to 6–11 kg. calories per gram of nitrogen. The work of renal excretion is, therefore, an important element in the specific dynamic action of protein.

Current views on the specific dynamic action of protein, whether derived from Rubner or Voit, look to one process only as responsible for the increased metabolism following the ingestion of protein. In this Zuntz,[2] who first ascribed the specific dynamic action of protein to the work of digestion and absorption, and later to the work of excretion of nitrogen, held in this respect essentially a similar position.

The purpose of the present communication is to show that the course of the specific dynamic action of protein parallels the course of nitrogen excretion; and in the well-nourished animal is the result of at least two processes, of which one is the work imposed upon the kidney, and the other is what may be called the "specific dynamic action proper," due to the metabolism other than excretion of the nitrogen, and of the carbon.

In the majority of studies of the specific dynamic action of protein, the recorded observations, upon which the stated conclusions are based, cover a period in which a fraction only of the ingested nitrogen was accounted for, and the magnitudes of the increases in metabolism obtained have been referred to the total weight, or amount of nitrogen ingested. If the specific dynamic effects of two substances, glycine and glutamic acid for example, are compared, one of which is absorbed and metabolized quickly, the other very slowly, and the data upon which the comparison is based are derived from observations during the first few hours, only, and if the comparison is referred also to the amount ingested, not metabolized, it is obvious that the substance metabolized more quickly, all other factors being the same, will appear to exert the larger specific dynamic effect. Nevertheless, differences in rate of metabolism often have

not been taken into account. When this factor is not omitted from consideration, the explanation of some hitherto anomalous phenomena becomes evident, viz.: the neutralization of the specific dynamic effect of glycine or alanine when administered with protein; the apparently low specific dynamic effect of glutamic acid; and the reduction of the specific dynamic action of protein in cases of endocrine disturbance.

A correlation between the amount of additional urea and ammonia excreted and the extent of the specific dynamic action has been controverted by Lusk and his pupils. Accordingly we have set out in figures 1, 2 and 3, and tables 1, 2 and 3, the data obtained on the dog, by Rapport,[3,8] Weiss and Rapport,[4] and Rapport and Beard[5] which, we believe,

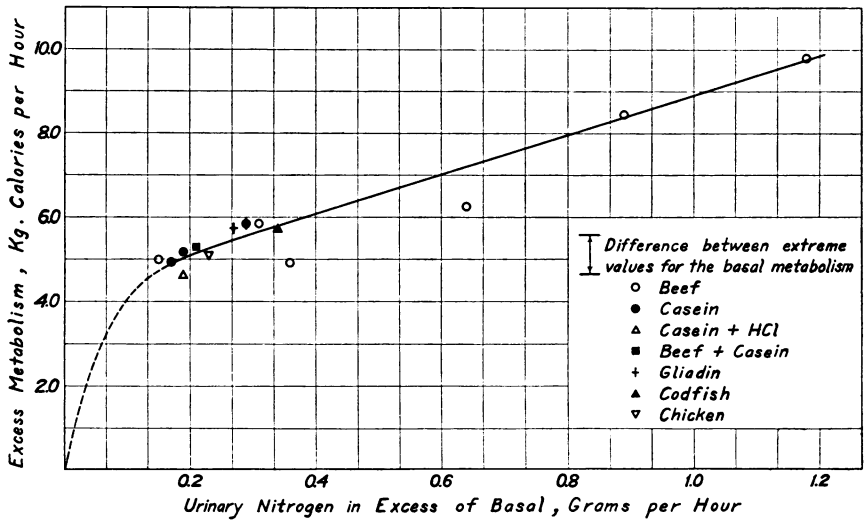

FIGURE 1

clearly demonstrate this correlation, although Rapport, and Weiss and Rapport stated that there is no clearly demonstrable relation between the nitrogen eliminated and the increase in metabolism.

The data have been arranged in three groups: one containing the results obtained with proteins only; another, the data on glycine, alanine and gelatin; and one containing the results with glycine, gelatin, and total and fractionated hydrolysates of gelatin. The later observations of Rapport and Beard[5] show the necessity for not including gelatin with the other proteins if just comparisons are to be made. Since a number of amino acids exert a greater specific dynamic effect, per gram of nitrogen excreted, than glycine or alanine, it is to be expected that the effect of most proteins in general will be greater than that of these two simple amino acids.

Gelatin, on the other hand, contains 26 per cent glycine, 9 per cent

alanine, and 25 per cent of the slowly absorbed dicarboxylic amino acids and leucine. It is low in phenylalanine and is lacking in tyrosine; both of these amino acids have higher specific dynamic effects per mol metabolized than glycine or alanine. It belongs, therefore, in respect of its specific dynamic action in the first few hours, more properly with glycine and alanine than with the proteins. The results given in tables 1 and 2 and figures 1 and 2 were obtained on the same dog; those in table 3, and figure 3, were obtained some time later on a different dog.

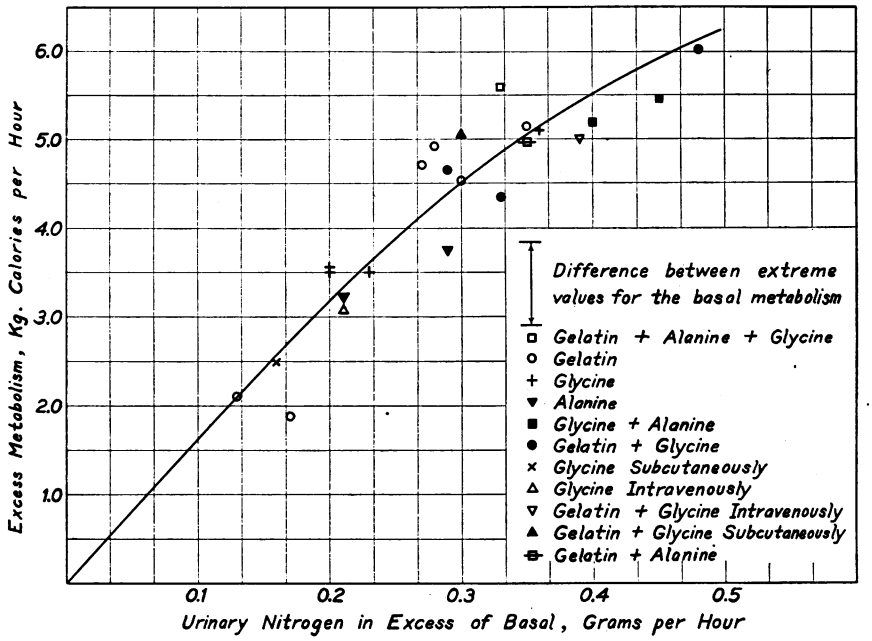

FIGURE 2

Figures 1, 2 and 3, and tables 1, 2 and 3 show the correlation between nitrogen excretion and excess metabolism. In view of the difficulty of the experimental technique, and of the variability of animals, the concordances of the results obtained by Rapport, Weiss and Rapport, and Rapport and Beard, is remarkably good. Figure 1, which is the most extended of the three curves, shows that the relationship between excess metabolism and excess nitrogen excreted is not defined by a straight line passing through the origin. The curve seems, rather, to begin from the origin as a steep curve, and to pass later into a straight line of distinctly lesser slope. This changing slope expresses in part the neutralization postulated by Weiss and Rapport[4] of the specific dynamic action of amino acids when these were added to relatively large quantities of protein. Weiss and Rapport compared the specific dynamic effects over the first

four hours of mixtures of gelatin and casein, and an amino acid, glycine or alanine, with the specific dynamic effects, over the same period of time of the same quantity of each of the substances when administered separately. The results observed were that the increase in metabolism was distinctly less than the linear sum of the effects of the protein and of the amino acid when administered separately. Weiss and Rapport concluded from these results that the specific dynamic effects of the amino acids were neutralized when administered with protein.

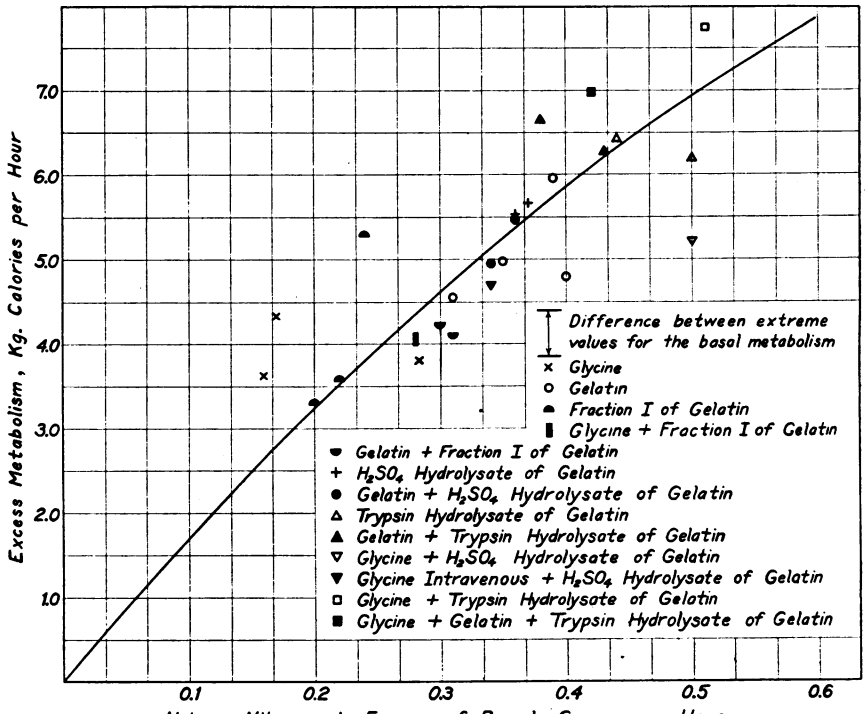

FIGURE 3

Figures 1, 2, and 3 show that an apparent neutralization of the specific dynamic action was obtained during the first four hours, whenever the quantity of nitrogen metabolized in this period was so large that it fell on the portion of the curve which does not pass through the origin when extended. This begins to be indicated when rather large quantities of amino acids were given, for which no neutralization phenomenon was postulated, and is clearly shown also when increasing quantities of beef were administered.

The data of Weiss and Rapport show an increase in metabolism, after the ingestion of 1.87 gm. of glycine, of 21.4 per cent; when an additional

1.87 gm. of nitrogen in the form of glycine were given, the increase over the basal was 30.9 per cent; and when 1.55 gm. of nitrogen in the form of gelatin were given with 1.87 gm. of glycine nitrogen, the increase in metabolism over the basal was 26.5 per cent. The increase in metabolism for this amount of gelatin alone was 12 per cent. Therefore, when the bolus ingested was increased by additional glycine or gelatin, the effect obtained was less than a linear sum of the separate specific dynamic effects; and the effect of the glycine-gelatin mixture was substantially the same as when the same amount of nitrogen was given in the form of glycine. Here, therefore, glycine exerted a neutralizing effect upon itself, similar to that

TABLE 1—(See Figure 1)

THE RELATION BETWEEN THE EXCESS NITROGEN EXCRETED AND THE SPECIFIC DYNAMIC ACTION OF PROTEIN (3) (4)

SUBSTANCES INGESTED	NITROGEN EXCRETION IN EXCESS OF BASAL PER HOUR GM.	METABOLISM INCREASE OVER BASAL, PER HOUR CALORIES	METABOLISM INCREASE OVER BASAL PER CENT
Beef	0.15	4.99	30.3
	0.29	5.86	35.6
	0.31	5.86	35.6
	0.37	4.92	29.8
	0.64	6.27	38.1
	0.89	8.43	51.2
	1.18	9.81	59.5
Casein	0.17	4.93	29.9
	0.19	5.18	31.4
Casein + HCl	0.19	4.65	28.2
Beef + Casein	0.21	5.29	32.1
Gliadin	0.27	5.76	35.0
	0.29	5.88	35.7
Codfish	0.34	5.73	34.8
Chicken	0.23	5.11	31.0

postulated when larger amounts of gelatin were given with glycine. When the amounts of nitrogen ingested and metabolized in the first four hours were larger, the neutralization was more marked.

A second factor in the phenomenon of neutralization is that the relationship between nitrogen ingested and nitrogen metabolized, i.e., excreted, is similarly not represented by a straight line, but by a curve of diminishing slope. For instance, the excess nitrogen excreted during the four-hour period after the ingestion of 10 gm. of glycine was 0.21 gm. per hour; after 20 gm. of glycine, 0.36 gm.; after 10 gm. of gelatin the excess urinary nitrogen was 0.15 gm.; after 40 gm. of gelatin, 32 gm.

When the exciting substances are similar, though not necessarily identical, the same increase in metabolism was obtained when the amount of nitrogen metabolized was the same. This is shown in the following

experiments of Weiss and Rapport. When 6 gm. of nitrogen were administered in the form of gelatin, there was an increase in the urinary nitrogen of 0.30 gm., and a 29.3 per cent increase in metabolism. In another experiment, when 6 gm. of nitrogen in the form of gelatin and 1.87 gm. of nitrogen as glycine were given together, the increased urinary nitrogen was 0.29 gm. and the increase in metabolism, 28.2 per cent. The apparent neutralization in this case of the specific dynamic effect of glycine is obviously due to some slowing of the rate of metabolism of

TABLE 2—(See Figure 2)

THE RELATION BETWEEN THE EXCESS NITROGEN EXCRETED AND THE SPECIFIC DYNAMIC ACTION OF ALANINE, GLYCINE, AND GELATIN (3) (4)

SUBSTANCES INGESTED	NITROGEN EXCRETION IN EXCESS OF BASAL PER HOUR GM.	METABOLISM INCREASE OVER BASAL PER HOUR CALORIES	METABOLISM INCREASE OVER BASAL PER CENT
Gelatin + Glycine + Alanine	0.33	5.58	33.9
Gelatin	0.13	2.09	12.7
	0.17	1.88	11.4
	0.27	4.71	28.6
	0.28	4.93	29.9
	0.30	4.53	27.5
	0.35	5.14	31.2
Glycine	0.20	3.51	21.4
	0.20	3.57	21.7
	0.23	3.50	21.2
	0.36	5.09	30.9
Alanine	0.21	3.21	19.5
	0.29	3.76	22.8
Glycine + Alanine	0.40	5.19	31.5
	0.45	5.46	33.1
Gelatin + Glycine	0.29	4.64	28.2
	0.33	4.36	26.5
	0.48	6.03	36.5
Glycine (subcutaneous)	0.16	2.48	15.1
Glycine (intravenous)	0.21	3.07	18.6
Gelatin + Glycine (intravenous)	0.39	5.01	30.4
Gelatin + Glycine (subcutaneous)	0.30	5.07	30.8
Gelatin + Alanine	0.35	4.98	30.2

the mixture, and not to a neutralization of the specific dynamic effect of glycine, *per se*. When large amounts of protein or amino acids or mixtures of the two are ingested there is a superposition of two non-linear effects; one is that the relationship between nitrogen ingested and nitrogen metabolized is not a linear function; the other, that the relationship between nitrogen metabolized and the increase in energy metabolism, over the first four hours, is also less than linear.

The term neutralization for this phenomenon implies that the specific

dynamic effects of these amino acids would be absent even when all the nitrogen ingested was accounted for in the urine. In the experiment in which glycine was administered with casein, during the first four-hour period of the experiment, only 14 per cent of the ingested nitrogen was excreted; in the case of casein and alanine, 12 per cent; gelatin and alanine,

TABLE 3—(See Figure 3)

THE RELATION BETWEEN THE EXCESS NITROGEN EXCRETED AND THE SPECIFIC DYNAMIC ACTION OF GLYCINE, GELATIN AND GELATIN HYDROLYSATES (5) (8)

SUBSTANCES INGESTED	NITROGEN EXCRETION IN EXCESS OF BASAL PER HOUR GM.	METABOLISM INCREASE OVER BASAL PER HOUR CALORIES	METABOLISM INCREASE OVER BASAL PER CENT
Glycine	0.16	3.62	29.2
	0.17	4.33	34.9
	0.28	3.79	27.7
Gelatin	0.31	4.56	36.8
	0.35	4.98	40.2
	0.39	5.96	43.6
	0.40	4.81	35.2
Fraction I of Gelatin	0.20	3.31	26.7
	0.22	3.60	29.0
	0.24	5.31	42.8
Glycine + Fraction I of Gelatin	0.28	4.06	32.7
Gelatin + Fraction I of Gelatin	0.30	4.21	34.0
	0.31	4.08	32.9
H_2SO_4 Hydrolysate of Gelatin	0.36	5.53	40.5
	0.37	5.67	41.6
Gelatin + H_2SO_4 Hydrolysate of Gelatin	0.34	4.96	36.3
	0.36	5.48	40.1
Trypsin Hydrolysate of Gelatin	0.44	6.42	47.0
	0.50	6.20	45.4
Gelatin + Trypsin Hydrolysate of Gelatin	0.38	6.64	48.6
	0.43	6.27	45.9
Glycine + H_2SO_4 Hydrolysate of Gelatin	0.50	5.22	38.2
Glycine (intravenous) + H_2SO_4 Hydrolysate of Gelatin	0.34	4.71	34.5
Glycine + Trypsin Hydrolysate of Gelatin	0.51	7.75	56.7
Glycine + Gelatin + Trypsin Hydrolysate of Gelatin	0.42	6.98	51.1

16 per cent; gelatin and glycine, 10 gm. of each, 39 per cent; and of a mixture of gelatin, glycine and alanine, 13 per cent. The effects observed obviously relate only to rates of absorption and metabolism; the data do not permit of any conclusions regarding absolute effects.

If the observations during the first four hours are confined to quantities

of nitrogen not more than 0.3 or 0.4 gm. per hour greater than the basal, the curvature is such that there is not a wide departure from a linear relationship between excess metabolism and nitrogen excreted in excess of the basal. For instance, the results in tables 2 and 3 depicted in figures 2 and 3 yield a relatively constant value of approximately 16 kg. calories per gram of nitrogen excreted in excess of the basal. The results of Wilhelmj and Bollman[6] confirm this conclusion. These authors concluded from their observations on the effects on metabolism of injected glycine, alanine and phenylalanine that "The relationship between the specific dynamic action may be expressed in at least six different ways, and reasons are given for believing that the most suitable manner of expressing this relationship is as calories and extra heat produced by each millimol of the amino acid deaminized." In a later paper Wilhelmj and Mann[7] present further experimental evidence in support of this correlation.

The results plotted in figures 1, 2 and 3 are the individual observations, when these are given; the alignment of points is distinctly better if averages only are used; the widest divergence from the mean position of the points is usually little greater than the difference between the extreme values for the basal metabolism.

It is interesting that the slope of the straight line portion of figure 1 yields a value for the increase in metabolism per gram of excess urinary nitrogen of 5 kg. calories, which is of the same order of magnitude as the energy consumption of the kidney observed in man, per gram of urinary nitrogen. This coincidence suggests the following possible interpretation of the results given above. The specific dynamic action of protein or amino acids, at any given time, is an expression of the resultant of two rates, of which one is the excretion of nitrogen, and the other, the metabolism and probably also the formation of the deaminized residues. The first steep part of figure 1, which corresponds to nearly the whole of figures 2 and 3, represents these combined effects. The flattening of the curve is due to the attainment of a maximum rate of deamination and metabolism of the deaminized fragments. Once this maximum intensity of metabolism is attained, this factor no longer contributes to the slope of the curve. The continuing straight line portion expresses the metabolism of the kidney. The persistence of the slope unchanged indicates that the rate of urea excretion can be increased by the ingestion of increasing amounts of protein, long after the maximum rate of metabolism of the deaminized residues has been attained; and that the excretion of nitrogen lags behind deamination.

The hypothesis advanced here is based chiefly on observations made over the first four hours following the ingestion of proteins or amino acids. The fact that even in this short period processes with different rates are discernible indicates that if a sufficiently large number of observations

over a longer period were available, further complications would be observed, due, for example, to the completion of some processes and the continuance of others.

Further evidence of the association of the specific dynamic action of protein with nitrogen metabolism is contained in the observations of Wishart[9] on the variations in the basal metabolism with changes in the nitrogen excretion, resulting from the variations in the daily protein intake. During the period of observation the daily nitrogen excretion varied in one subject from 5.3 gm. to 23.2 gm., and in another from 3.8 gm. to 16.5 gm. The results obtained could be expressed by the equations $x = 28.456 + 0.449y$ in the one case, and in the other by $x = 28.269 + 0.448y$; where x is the basal metabolism in calories per square meter per hour, and y the urinary total nitrogen in g. per day. The correlation coefficients were, $+0.84 \pm 0.036$, 0.70 ± 0.05. These results show a linear relationship between nitrogen excretion and increase in metabolism. The coefficient of y is of the same order of magnitude as that for the first part of figure 1, or for figures 2 and 3, which includes the effects of the metabolism of nitrogen and the deaminized fragments. This is in accord with the results obtained on dogs because even the largest amount of nitrogen metabolized here corresponds to points on the lower portions of figure 1, or figures 2 and 3. For instance, 23.2 gm. of nitrogen per day would correspond in a 20-kg. dog to about 0.3 gm. per hour. As pointed out above, in this range of excess nitrogen excreted the specific dynamic effects observed on the dog are defined approximately by a linear function of the amount of nitrogen excreted in excess of the basal.

The observations in cases of endocrine disturbance, also show the relationship between nitrogen metabolism and the specific dynamic action of protein. Liebeschütz-Plaut[10] noted a reduction in the specific dynamic action of protein in cases of *dystrophia adiposogenitalis*. This was confirmed by Liebesny[11] on men, and by Foster and Smith[12] on hypophysectomized rats. Gaebler[13] in Lusk's laboratory compared the specific dynamic effects of meat, in the dog, before and after hypophysectomy; and found before the operation an average increase in excretion of nitrogen per hour, after a meat meal, of 0.16 gm., and an increase in metabolism of 4.4 calories per hour; after the hypophysectomy the average increase in nitrogen excretion (over the normal basal value, which is probably too high in this case) was 0.09 gm. per hour, and the increase in metabolism 3.2 calories per hour. Gaebler's conclusion was that "discrepancies in the amount of protein catabolized probably account for the difference in the extent to which the heat production was increased in the two animals." Lusk's summary of the findings in this condition,[24] shows that the general rate of metabolism is lowered after hypophysectomy or pituitary deficiency. Foster and Smith found that the metabolism in these animals

may be restored to normal by anterior pituitary homotransplants, or by daily injections of thyroid extract.

Taken in conjunction with Gaebler's experiments, the findings in case of hypophyseal deficiency indicate no real reduction in the specific dynamic action, but rather a slowing of the rate of metabolism. Per gram of nitrogen metabolized, the specific dynamic action is the same as in the normal. Lauter[14] showed that in the case of obese individuals the specific dynamic action of protein is less, during the first two hours, than in normal individuals, but is the same as in the normal over a period of six hours.

The correctness of the association of the extent of the specific dynamic action with the nitrogen metabolism, i.e., with the increase in urinary nitrogen, is consistent with the time relationships. Lusk reproduces in "The Science of Nutrition" a curve from the data obtained by Aub and Dubois on human beings, which shows the concomitant increases in urinary nitrogen, urinary sulfate, and in the rate of metabolism. Another similar curve is reproduced from the data of Williams, Riche and Lusk. It may be added that, following the ingestion of some proteins, there is an increase also in urinary phosphate. The excretion of sulfate and of phosphate imposes work upon the kidney, in much the same manner, though to a lesser extent in the case of protein, as in the excretion of urea; and therefore, also figures in the specific dynamic action of protein.

The observations of Wilhelmj, Bollmann and Mann[15] that injected amino acids do not exert any specific dynamic effect in hepatectomized dogs, definitely eliminates the view that the specific dynamic action of amino acids is due to a general stimulation of the cells of the body by the amino acids *per se*. The earlier observations of Rapport and Katz[16] of an increase in metabolism following the addition of glycine to the circulating blood of an isolated hind leg preparation is open to the criticism that the concentration of glycine in the circulating blood was relatively enormous, about one per cent. The difficulty of interpreting this observation of Rapport and Katz is further increased by the recently reported observations of Needham[17] that neither glycine nor alanine increased the respiration of a minced muscle preparation, though a marked increase was observed with glutamic acid.

The observations of Grafe[18] that ammonium chloride and acetamide exert a large specific dynamic effect, with the failure of the amino acids to provoke an increase in metabolism in the hepatectomized animal, and the general correlation of the increase in metabolism with the increase in urinary nitrogen, indicate that either the whole or part of the composite process of urea formation and excretion are responsible for a large fraction of the specific dynamic action of protein.

The view that the specific dynamic action of protein is due to the

formation of glucose from the deaminized fragments chiefly of glycine and alanine is again put forward by Chambers and Lusk in a recent paper.[22] This proposal meets with the difficulty of accounting for the important observation of Rapport[3] that the specific dynamic action of a variety of proteins is nearly the same, and was lowest among the proteins tried for gelatin, which contains the most glycine and alanine, and was highest for gliadin which contains over 40 per cent glutamic acid and very small amounts of glycine and alanine.

In this paper, Chambers and Lusk reassert the contention that no specific dynamic action is exerted by glutamic acid. Grafe, Rapport and Beard, and Terroine and his collaborators[19,20] have reported that glutamic acid exerts a considerable specific dynamic action. Johnston and Lewis[23] observed that glutamic acid, administered to rabbits *per os*, was absorbed very slowly compared to alanine and glycine. On the other hand, injected intravenously glutamic acid was deaminized as quickly as alanine or glycine. Rapport and Beard, from their own observations, suggested that the apparently low specific dynamic effect of glutamic acid is due to the slowness of its absorption. The data in the protocols of Chambers and Lusk suggest that this discrepancy may be resolved by considering the amount of glutamic acid deaminized during the period of observation. In one experiment, the data of Chambers and Lusk show that in the third hour after the ingestion of 20 gm. glutamic acid by a normal dog, with an increase in urinary nitrogen of only 0.03 gm. per hour, the metabolic rate was 1.8 per cent lower than the average basal value. In three other experiments, when the same amount of glutamic acid was given with 10 gm. lard (the specific dynamic action of which is only 3.5 per cent and which alone induced no increased excretion of nitrogen), during the second and third hours there was an increase in the hourly urinary nitrogen of 0.1 gm., accompanied by an increase in the metabolic rate of 15 per cent. The difference between the rate of absorption and metabolism of glutamic acid as compared with other amino acids is illustrated in the effect on the same dog of 300 gm. lean meat. The hourly urinary nitrogen was increased eight-fold, and the metabolic rate 52.3 per cent.

After these observations were made the animal was phlorhizinized and glutamic acid again administered; from the results obtained, Chambers and Lusk concluded that there was no specific dynamic action of this amino acid in the phlorhizinized animal. The values of the basal metabolism, 26.5 calories per hour, with which the glutamic acid figures were compared, is an average of the following values obtained on the days of the experiments: 23.4, 29.4 and 26.7. It is not possible from the urinary nitrogen figures, which were also irregular here, to obtain a reliable estimate of the amount of glutamic acid deaminized, except that it was small.

The strongest evidence upon which the theory suggested by Lusk is

based, that the specific dynamic action is due to the conversion of the deaminized residues of the amino acids into glucose, is derived from the observations that the specific dynamic action of glycine and alanine is the same in the phlorhizinized dog, as in the normal animal. In the interpretation of this result, Lusk assumes that the phlorhizinized dog is unable to burn glucose, and that the glycine and alanine ingested are converted quantitatively into glucose. In Lusk's summary[24] of the effects of phlorhizin, the observations of Richardson and Shorr are quoted that the excised tissues of phlorhizinized rats burn glucose as freely as the normal; and further, that a variable quantity of ingested glucose is oxidized by the phlorhizinized animal. As Terroine and Bonnet[25] have pointed out in their discussion of this problem, even in the normal animal glucose probably is not oxidized as such, but in the form of some degradation product such as lactic acid. An alternative and equally tenable interpretation, therefore, of the observations on the phlorhizinized dog is that the deaminized fragments of the amino acids are oxidized by the phlorhizinized dog in place of degradation products derived from glucose, with the result that an amount of glucose is spared from combustion, and is thereby excreted in the urine, which is approximately equivalent to the ingested amino acids. This would tend to lessen the total metabolic rate in the phlorhizinized as compared with a normal animal. On the other hand this is compensated for by the increase in the renal work, and hence the total metabolism, by the excretion of an increased amount of glucose.[1] The magnitude of this increase will be of the same order as the energy consumed by the kidney in the excretion of the nitrogen.

In their paper, Chambers and Lusk return to a discussion of the energy changes in the hypothetical conversion of glycine, alanine and glutamic acid into glucose and urea. The following equations are written:

for alanine: $2C_3H_7NO_2 + H_2O + CO_2 \longrightarrow C_6H_{12}O_6 + CON_2H_4$;

for glycine: $3C_2H_5NO_2 + {}^3/_2CO_2 + {}^3/_2H_2O \longrightarrow C_6H_{12}O_6 + {}^3/_2O_2 + {}^3/_2CON_2H_4$;

and for glutamic acid:

$$2C_5H_9NO_4 + 3O_2 \longrightarrow C_6H_{12}O_6 + H_2O + CON_2H_4 + 3CO_2.$$

The calculations of Adams[26] are referred to, who, with the aid of the Third Law of Thermodynamics, estimated that approximately 60,000 calories would be required to effect the change of state indicated above for alanine. The specific heat data at present available are too scanty to permit of reliable estimates of the entropies of alanine and of glycine. Accordingly, calculations of the free energy change incurred in the conversion of glycine to glucose and urea, although the standard free energies of glucose and urea are now known, are at present uncertain. An estimate

of the direction and magnitude of the energy change can be obtained by means of the First Law of Thermodynamics. From the data in the International Critical Tables, the following values have been calculated for the molar heats of formation: water, −68,000 calories; carbon dioxide, −94,000 calories; glucose (solid), −303,000 calories; urea (solid) −79,000 calories; glycine (solid), −126,000 calories; alanine (solid) −134,000 calories; and glutamic acid (solid) −237,000 calories. The value of $-\Delta H$ in the reaction postulated above for alanine is −24,000 calories per mol; for glycine, −66,000 calories; and for glutamic acid +129,000 calories. The values for the alanine and glycine reactions are nearly the same as those given by Adams.

Assuming for a moment the reality of these reactions, it may be concluded from the above values of $-\Delta H$, that the conversion of glycine and alanine into glucose and urea are endothermic processes requiring the driving force of another exothermic process. And if it is assumed that the relationship is not perfectly reversible between the endothermic and exothermic processes, the specific dynamic action will be the difference between the amount of energy produced and the amount used in the endothermic reaction. There are no data for estimating the degree of reversibility of such a reaction in the body. If a 25 per cent efficiency is assumed, then the specific dynamic action per mol of glycine would be approximately 200,000 calories. This is the order of magnitude of the specific dynamic action of glycine. But on the same basis, the specific dynamic action of alanine should be one-third that of glycine. The experiments of Lusk, and of Wilhelmj and Bollman, and of Wilhelmj and Mann are in accord that the specific dynamic action of alanine per mol of amino acid deaminized is practically the same as that of glycine. $-\Delta H$ for glutamic acid is positive; the reaction is, therefore, exothermic. The value of $-\Delta H$, moreover, is quite large, equivalent to the heat of combustion of $^1/_5$ mol glucose. There is no obvious justification for assuming, as do Lusk, and Aubel,[30] that because this reaction is itself exothermic, that it is not responsible for any specific dynamic action. Rather the reverse, it seems that this is the one reaction of the three which would certainly exert a specific dynamic effect. Even in the cases postulated for glycine and alanine the specific dynamic action is due to exothermic processes. As pointed out above, gliadin, which contains over 40 per cent of glutamic acid, exerts a large specific dynamic effect. In this connection reference may be made to the observation of Terroine and Bonnet that the whole of the heat of combustion of ingested alcohol can be recovered as heat evolved by the organism.[27]

Furthermore, the values of $-\Delta H$ calculated for the above reactions include the energy changes for deamination and urea formation. There is no *a priori* reason for considering that the latter reactions and the excre-

tion of urea are negligible in the energy balance. The failure of sodium lactate and sodium glycollate to exert a large specific dynamic action[21] might be taken to indicate that the formation of glucose from the deaminized residues of the amino acids is a negligible element. In the case of glycine and alanine, also, the mechanism postulated for the formation of urea (the dehydration of ammonium carbamate) has been severely criticized on chemical grounds by Werner.[28] If urea normally appears by way of cyanic acid from the concomitant oxidation of the amino acids and glucose,[29] the metabolism of glycine and alanine probably are exothermic instead of endothermic processes. This criticism of the view of Lusk and Aubel[30] regarding the cause of the specific dynamic action of protein has many points in common with the views of Terroine and Bonnet.

The values obtained for the specific dynamic action of the amino acids show that the work of the kidney in eliminating nitrogen cannot be responsible for the whole of the increase in metabolism. It was shown that the excretion of nitrogen in man incurs an expenditure of 6–11 kg. calories per gram of nitrogen.[1] In experiments in which most of the injected amino acid was accounted for, Wilhelmj and Bollman obtained in dogs the following values, expressed as kg. calories per gram of amino acid deaminized: for glycine, 35, 29 and 21; for alanine, 22, 28 and 20; and for phenylalanine, 56 and 44. In the later experiments of Wilhelmj and Mann, the values obtained for glycine were 16 and 18; and for alanine, 16 and 19. The few observations on the effect of tyrosine suggest that the specific dynamic action of this amino acid, per gram of nitrogen metabolized, is greater than that of phenylalanine. The data of Rapport, Weiss and Rapport, and of Rapport and Beard give somewhat low values for glycine, in accord with the lower values for glycine and alanine obtained by Wilhelmj and Mann. The values for glutamic acid obtained by Rapport and Beard are nearly as great as those of phenylalanine; but in these experiments only a small fraction of the ingested amino acid was accounted for.

If the specific dynamic action of protein were due only to the energy released in the deamination, formation, and excretion of urea, the specific dynamic action would be practically the same per mol for all the monoamino acids. Terroine and Bonnet found in the frog that, per gram of nitrogen injected, the specific dynamic action of glycine, alanine, aspartic acid, glutamic acid, valine, leucine, cystine and lysine was approximately 8.4 calories; for tyrosine and phenylalanine, 9.2 calories; and for tryptophane and histidine, 10 calories.[31] It is interesting and possibly significant, in view of these low values, that in the urine of the frog the concentration of nitrogen is practically the same as the non-protein nitrogen of the blood,[32] so that no additional work is imposed upon the kidney by the ingestion of proteins or amino acids, and hence in the frog the

specific dynamic action of amino acids might be predicted to be 6–11 kg. calories per gram of nitrogen less than in the mammal. Terroine and Bonnet[25] observed similar values in the rabbit. But the values obtained by the French observers on the rabbit may be too low if they are taken to signify the specific dynamic action per gram of nitrogen excreted in the dog or man. For instance, 16 gm. of glycocoll were injected into a rabbit weighing 2.7 kilos. The observations were made over a period of six hours, and it is improbable that in this time such a relatively very large quantity of the nitrogen was completely metabolized and excreted. On the other hand the energy consumption during renal excretion in the rabbit is probably less than in the dog or man.[1] The evidence favors acceptance of the higher values, in the case of the higher animals, obtained by Lusk, Weiss and Rapport and by Wilhelmj and Mann.

It is possible that the difference in the specific dynamic effects of different monoamino acids may be due to the metabolism of the varying number of carbon atoms which they contain. This would account for the greater specific dynamic effect, per mol metabolized, of phenylalanine, tyrosine and glutamic acid. But the data available are too incomplete for analysis.

An estimate of the value of the specific dynamic action of protein, as distinguished from that of an amino acid, can be derived from the observations of Wishart on man, referred to above. The equations of Wishart expressed as calories per hour, instead of calories per square meter per hour, are:

$$x = 52.65 + 0.83y,$$

and

$$x = 48.0 + 0.76y.$$

Taking y as gm. of nitrogen excreted per hour, the equations become:

$$x = 52.65 + 20y,$$

and

$$x = 48.0 + 18y.$$

The coefficients of y, 20 and 18, represent the increase in metabolism per hour per gram of nitrogen excreted. It is confirmatory of the explanation of the specific dynamic action of protein proposed here, that these values for the increase in metabolism induced by protein, calculated from changes in the basal rate with changes in the nitrogen excretion, are of the same order of magnitude as those calculated from the directly observed specific dynamic action of protein. These figures carry additional weight because the errors due to long periods of observation or to incomplete metabolism of the ingested protein could not occur here.

The results obtained indicate that the additional work imposed upon the kidney is responsible for 25–60 per cent of the specific dynamic action of protein and amino acids. The remainder is due to the "specific dynamic action proper" resulting from the metabolism of the nitrogen and of the

carbon. In this estimate it is assumed that the energy consumed by the kidney in the excretion of nitrogen is approximately the same in the dog as in man, in spite of the lower values of the dog obtained by Steck.[2] No details are given in the quotation of Zuntz regarding Steck's experiments; while the oxygen consumption values for the dog's kidney during urea diuresis indicate that the work of the kidney in the excretion of nitrogen is approximately the same in the dog as in man.[1]

The values obtained for the increased energy consumption by the kidney in man, per gram of nitrogen excreted indicate that increased renal function may be responsible for as much as 40 per cent of the specific dynamic action of protein observed in man by Aub and Dubois.

Summary.—Taken in conjunction with the data on the efficiency of the process of renal excretion, analyses of the data bearing upon the relation of the increase in metabolism following the ingestion of protein or amino acids reveals:

(1) A close correlation between the specific dynamic action of proteins or of amino acids and the increase, over the basal level of excretion, in the urinary nitrogen;

(2) That neither the direct experimental evidence nor the considerations of the energy relations support the view that the specific dynamic action of protein is necessarily due to the conversion of the deaminized fractions into glucose.

(3) The values of the specific dynamic action of amino acids and of proteins indicate that 25–60 per cent is due to the work imposed upon the kidney. The remainder of the specific dynamic action of protein or amino acids is due to the metabolism of the nitrogen and the carbon, though it is not possible, from the evidence, to estimate the proportion for which each is responsible.

(4) This hypothesis, that the specific dynamic action of protein is due to at least two distinct processes, which do not proceed at similar rates, provides an explanation for some hitherto anomalous phenomena in the specific dynamic action of protein.

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THE CALIFORNIA EARTHQUAKES OF NOV. 28, 1929, AND THE SURFACE LAYERS OF THE EARTH IN CALIFORNIA

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On November 28, 1929, at about 11h. 49m. A.M., Pacific Standard Time and again about 3 minutes later, the west central section of California and the adjoining portion of Nevada were shaken by earthquakes which attained an intensity of about VII, Rossi-Forel scale, about 5 miles southeast of Aberdeen, California. Here the earthquakes cracked concrete reservoirs, broke plates on shelves and overturned an alarm clock. At the head of Goodale Creek, some 20 miles southwest of Bishop, a large landslide occurred at the time of the earthquakes. According to one report, "considerable of south side of mountain top slid down into gorge on the headwater of Goodale Creek about $1^1/_2$ miles north of Division Creek Power House." This landslide was photographed from an airplane while it was taking place. The photograph is in the hands of Prof. J. C. Jones